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EVALUATION OF AEROSOLIZED MEDICATIONS DURING PARABOLIC FLIGHT MANEUVERS

ND185000

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FLIGHT DATES:	March 27, 1990

EXECUTIVE SUMMARY

The goal of this experiment was to visually evaluate the effect gravity has on delivery of medications by the use of various aerosol devices. To assist the visual inspection of the devices, high speed video or film was to be considered. During the preliminary ground testing in the studio it was concluded that high speed video would not be capable to provide sufficient resolution of the aerosolized mist. After evaluation of the high speed film ground test data it was determined that the ideal film speed would be 250 FPS using a 50 mm lense.

During parabolic flight the same four aerosols were retested as performed in the studio. It appears that the Cetacaine spray and the Ventolin inhaler function without failure during all test. The pump spray (Nostril) appeared to function normally when the container was full however it appeared to began to fail to deliver a full mist with larger droplet size when the container was nearly empty. The simple hand spray bottle appeared to work when the container was full and performed progressively worse as the container was emptied.

During the Apollo flights they reported that "standard" spray bottles proved to be unsatisfactory, however they did not indicate why. It appears that we would also conclude that "standard" spray bottles do not function as well in zero-g by failing to produce a normal mist spray. The standard spray bottle allowed the fluid to come out in a narrow fluid stream when held with the *nozzle either level or slightly titled upward.

INTRODUCTION (Justification):

This proposal outlines a procedure designed to evaluate the utility of selected aerosolized medication devices under zero gravity conditions during KC-135 parabolic flight. Results obtained from this experiment would be extrapolated to the situation of a continuous micro-g environment, such as aboard Space Station Freedom. There is concern that such devices may be inconsistent in their delivery of the manufacturer's preset quantity of drug per unit of use (i.e., inhalation, puff, nozzle depression) under zero-g conditions. The current draft of the HMF pharmaceutical formulary contains three aerosol preparations:

1. Benzocaine 20% (topical anesthetic)
2. Albuterol (bronchodilator)
3. Nitroglycerin (vasodilator)

GOAL:

To determine if delivery of medications through use of an aerosolizing device is an acceptable method of drug delivery in a zero-g environment.

OBJECTIVES:

1. Compare patterns of spray dispersion under control (1-G) and zero-G conditions).

2. Determine total available quantities of drug for each delivery system under control (1-G) and zero-G conditions.

MATERIALS AND METHODS (Approach):

MATERIALS

Flight Crew

Three people shall be required. One investigator will work inside the glove box while the other person shall manage exchange of materials from the storage bags to the glove box.

- C. Lloyd (CL)
- J. Gosbee (JG)
- High Speed Film support

Drugs

1. Benzocaine 14%, Butyl Aminobenzoate 2%, Tetracaine Hydrochloride 2% topical Anesthetic Spray (Cetacaine), manufactured by Cetylite Industries. Average expulsion rate is 200 mg per second, (Quantity = 2 bottles). 56 gm net weight. Also contains Benzalkonium chloride 0.5% and Cetyl dimethyl ethylammonium bromide 0.005%. Lot #299-4, Exp Date 6/91.

2. Microcrystalline suspension of albuterol Inhaler (Ventolin) 17 gm, Allen & Hanburys, Division of Glaxo Pharmaceuticals, 200 metered inhalations, 90 mcg/actuation, (Quantity = 2). Also contains Trichloromonofluoromethane and dichlorodifluoro-methane. Lot #Z13679HA, Exp Date FEB 92. (Quantity = 2)

3. Phenylephrine HCl 0.25% (NOSTRIL) Nasal Decongestant, Metered one-way pump spray, 15 mL, Boehringer Ingelheim. Also contains Benzalkonium chloride 0.004%, Boric acid, Sodium borate, and water. Lot #839001A, Exp Date JUL 92. (Quantity = 2)

4. Oxymetazoline HCl 0.05% (GENASAL), AFRIN generic, nasal decongestant spray, 30 mL, Goldine Laboratories. Also contains Phenylmeric acetate 0.02 mg/mL.Exp Date APR 92. (Quantity = 2)

KC-135 Working Space Requirements

1. Forward in the aircraft.

2. Full width of the plane

3. At least 12 feet in length.

NOTE:

Justification for this set up is to allow for the camera(s) to be fixed mounted and blackout curtains placed around the lense(s) to avoid any secondary lighting to effect the filming. There will be no real-time adjustments for the lenses positioning in-flight. To perform this type of filming the set-up also requires additional lighting to be in key positions around the glovebox.

Supplies

1. Glove box and supporting stand
2. Velcro material to secure drug products
3. Flat black absorbant cloth to line inside of glove box
4. Bungy cord to secure investigator in-flight
5. Duct Tape
6. Cleaning solution and towels

PROCEDURES (TO BE PERFORMED PRE- AND IN-FLIGHT)

Spray Dispersion

1. Shake pressurized container well
2. Hold the device in the appropriate orientation for administration of the drug product and depress the plunger (command given by photographer) to provide one to two actuations.
3. Positioning of the device by the investigator working in the glovebox will be determined pre-flight and marked inside the box. The high-speed photographer shall determine the
4. Repeat above procedure x 5 for each drug
5. Camera specs for PRE-FLIGHT testing performed in the building #8, JSC, Photography studio:

SHUTTER	*FPS*	*SIZE (mm)*	*#RUNS*
36	100	10	2 of #1
36	250	10	2 of #1
36	250	25	2 of #2
36	100	25	2 of #2
72	100	25	#1-4a
72	250	25	#1-4a
72	250	10	#1-4
72	100	10	#1-4
72	100	25	#1-4
72	250	25	#1-4

DRUG CODE:

#1 - Cetacaine
#2 - Ventolin
#3 - Nostril
#4 - Afrin (generic)

Not all lighting was turned on during the first filming therefore these two set-ups were repeated at the end.

6. Perform still photography if possible during the filming. If this is not possible then complete after all high-speeding filming hasbeen completed.

GROUND SUPPORT REQUIRED

Flight (CL and JG) and Ground (Dr. Martin, T Guess and A. Freemen) crews will need to obtain necessary supplies, prepare the test items, and perform 1 to 2 ground test pre-flight.

FLIGHT SUPPORT REQUIRED

The Ground crew will need to assist the flight crew with the set up of the glovebox on the plane pre-flight.

NUMBER OF FLIGHTS AND DATES DESIRED:

Number of flights: 2

Requested Dates:

- First quarter of 1990

Actual Flight Dates:

- March 27, 1990 (1 day)

PROJECTED RESULTS:

It is believed that the aerosols will perform properly until the pick-up stem of the canister begins to contain air/fluid mixture secondary to the micro-g environment. Afterwards the output should become erratic and not deliver a full dose of the medication.

Pre-flight (1-g testing) Results

1. Glovebox and supporting materials were taken to the photography studio in building #8 on February 20, 1990 for the pre-flight testing.

2. The objective of the pre-flight testing was to determine the appropriate film to be used, camera set-up requirements, lighting requirements and camera settings for the in-flight filming.

3. The pre-flight testing would also modify testing procedures and identify any additional material needs.

4. Both in-flight investigators had an opportunity to perform all in-flight procedures while test filming was being evaluated.

5. All test articles (drug products) were filmed.

6. Additional materials needed included:

   - Flat black cloth material to line the inside of the glovebox.

7. KC-135 positioning and space requirements identified:
   - Forward in the aircraft.
   - Full width of the plane
   - At least 12 feet in length.

8. When the Cetacaine spray bottle was turned upside done and actuated it failed tofunction properly as soon as the pick up straw emptied. The Ventolin Inhaler fails tospray properly within 2 puffs when operated upside down. The pump spray and standard spray bottles are also positional dependent and fail quickly when operated in the improper position.

9. Post shoot viewing of the film has been scheduled for Monday March 5, 1990, 8 am, building #8 to determine if further ground testing shall be required, finalize cameraset-up and specs, and in-flight procedures.

In-flight Results (March 27th)

Immediately prior to the flight velcro was placed inside the glove box directly behind the gloves. All aerosol containers and the containers were inspected and the fluid level was marked on each container. Also **bungy cords were set up to restrain the investigator's ankles while performing the testing in the box. White tape was used to mark hand positioning to assure proper focusing of the camera. The following revisions were made to the in-flight procedures:

1. The order containers tested would also be Cetacaine, Ventolin, Pump container, and then Standard spray bottle.

2. During the first set of parabolas each 1/2 empty aerosol container would be tested during to consecutive parabolas. during the first parabola the aerosol device could be filmed immediately after entering in to the zero-g portion of the parabola. During the second parabola the same device would be actuated multiple times during the zero-g portion of the parabola and filming would start in the last 10 seconds.

3. In all cases at least 3 actuations of the device would be attempted to be filmed.

4. Starting with the second set of parabolas a set of full aerosol devices

would be used and sprayed until empty.

Parabola Set #1:

During the first set of parabolas a large bottle of Windex window cleaner was filmed. Since the bottle is clear plastic with a green colored fluid it was felt it may assist us to understand what may be happening inside some of the other containers. The Windex bottle was approximately 75% empty at the time of testing which allowed for the fluid to move away from the pick up straw during the parabola. During the first of 2 parabolas the solution appeared to begin to entrain air and slowly began to migrate up the walls of the container away from the opening in the pick up straw. This movement and entrainment of air is believed to be secondary to the operator pumping the spray and occasional zero-g forces. By the end of the first parabola the majority of the fluid had moved up into the neck of the bottle and the device began to dysfunction. During the second parabola the investigator was instructed to swirl the fluid around prior to the filming. This resulted in excessive foaming and entrainment of air into the fluid. The device failed to function.

During the next three parabolas Cetacaine spray was tested. During all tests the device appeared to function as normal. The spray stream to remain continuous throughout each actuation. During parabolas 6 and 7 the ventolin inhaler was filmed with no notable failures.

The pump spray container was evaluated early and late during parabolas 8 and 9. The operator stated that the device appeared to fail as the Windex bottle did when the fluid had shifted up into the neck of the bottle. The failure was characterized as occurring sporadically and late in the parabola.

During parabola 10 the early phase of the parabola filming was completed using the standard spray bottle. The device appeared to function normally.

Parabola Set #2:

During the first 2 parabolas of the second set the standard spray bottle. It is believed that the camera lense was partially blocked by the blackout curtain. Starting with parabola 3 the full containers were used in the order outlined above. Filming was performed early the first parabola and late during the second parabola for each device. It appeared that all devices functioned without out failure except the standard spray bottle. When the standard spray bottle was used it was actuated either with the nozzle tip pointing slightly upward or outward with the tip level to the base of the glove box. This device appeared to function properly in a intermittent fashion. One of three types of spray patterned was noted:

1. Normal mist spray which forms a v-pattern was the spray leaves the nozzle. This usually occurred when the device was predominantly full and the nozzle tip was pointed slightly upwards.

2. A simple narrow stream of liquid. This occurred if the nozzle tip was pointed out level with the base of the glove box. It appeared to occur when the fluid moved up into the neck of the bottle.

3. Slight bubbling and little or no fluid. This occurred more and more as the bottle was used and the residual fluid volume was furthest from the nozzle tip.

Parabola Set #3:

During the third set of parabolas no high speed filming was performed to allow for still photography to be completed. During the first parabola of the third set the Windex bottle was retested. During the remainder of the parabolas the containers were all retested. It appears that in all cases other then the standard spray bottle the devices function normally.

Parabola Set #4

Testing and filming only occurred during the first 5 parabolas. At this point all containers were believed to be nearly empty. The Cetacaine and Ventolin Inhaler continued to function without a failure. The pump and standard spray bottles failed to function properly. In both cases the device would fail and then after several actuations the device would function properly.

Post-flight (1-g) Results

No further testing was required. Each container was emptied and the approximate volume recorded:

Partial Filled Containers

#1	Cetacaine	8 seconds continuous
#2	Ventolin	97 puffs
#3	Nostril	8/15 mL remained
#4	Afrin (generic)	1/30 mL remained

Full Containers

#1	Cetacaine	42 seconds continuous
#2	Ventolin	192 puffs
#3	Nasalcrom	6/13 mL remained
#4	Neo-Synephrine	2/15 mL remained

It was noted during the process of determining the remaining volume in these containers that the Ventolin bottles formed a white powder around the nozzle opening. It has been suggested that this accumulation of powder may result inless volume being delivered per actuation. It is suggested during further testing that this type of product only be actuated 2 to 10 times, then the container nozzle opening be wiped off and the bottle shaken.

DISCUSSION AND CONCLUSIONS:

After reviewing the film and photographs it was determined that pressurized aerosol containers appeared to function better than either the standard squeeze type or pump type bottles. Other than the filming of the Windex bottle we were unable to suggest a reason for this behavior.It was reported in the Biomedical findings of the ApolloProgram that the standard squeeze type dropper bottle did not function well, however there was no comments regarding the other type of aerosol bottles evaluated in this experiment.

It is suggested that during the second flight of this experiment the investigators should repeat using clear bottles. To fulfill this objective the Cetylite company has provided with Cetacaine bottles which are clear. Other types of spray bottles will be obtained from Calmar Dispensing Systems, makers of various sizes, shapes, and types of spray containers. This second flight will be projected for the FY 91 HMF KC-135 fight year.

During the post-flight evaluation it was discovered that we had not evaluated these 1-g positional sensitive containers in different positions during Zero-G. This testing will be answered during the second flight as a specific objective.

The function of flying containers which were either "partial filled" or "full" was to allow for efficient us of our flight time. However, this process has some problems. First it was not known what the actual volume of the containers were pre-flight nor what volume was used during flight. therefore it was not possible to address the impact of partially filled containers on overall usefulness as compared to use in a 1-G environment. It did become clear during the flight that pressurized containers functioned at various fills and to a lesser extent this was also true for the pump and standard spray bottles. During future flights it is recommended that comparisons be performed to the effects zero-g has on fluid sprayed in zero-g versus 1-g testing. These volumes then may suggest potential reduction in container usefulness in a micro-g environment. It would also be extremely helpful to perform 1-g versus zero-g actuations of a product like Ventolin which is report to deliver 90 mcg per actuation. This type of test would require the cooperation of the pharmaceutical house.

REFERENCES:

1. Biomedical findings during the Apollo Program

2. Calmar Dispensing Systems, Inc. Lee's Summit, Missouri 64081, 816/ 524-4160, Mary A. Murray, Sales Representative.

BUDGET SOURCE:

SD2, Medical Operations, HMF Project.

PHOTOGRAPHS:

S90-33958
Chuck Lloyd is seen secured to the floor with the use of bungy cords over his legs. He is seen evaluating the function of the Cetacaine Spray container inside the Glove Box. The glove box is a clear plexglass box with rubber gloves on either end for the operator to work from. The Cetacaine bottle can be seen actuated with a fine white spray projecting across the box. The Cetacaine topical Anesthetic Spray bottle contains 56 grams of

14% Benzocaine, 2% Butyl Aminobenzoate, and 2% tetracaine hydrochloride with propellants. The spray is activated by pressing downwards on the arm of a Jetco nozzle. This container is designed to delivers 200 mg of medication per second. This device never appeared to fail in flight either early or late in the parabola. Walter Cunningham is seen looking on.

S90-33959
This photograph shows Chuck Lloyd operating the Ventolin (albuterol) Inhalation Aerosol device. This device holds 17 grams of a microcrystalline suspension of albuterol in a trichloromonofluoromethane & dichlorodifluoromethance propellant. The device delivers 90 mcg of albuterol at the mouthpiece per actuation. The shot does not show the actuation of the inhaler, however this device appeared to work properly throughout the flight as observed on high speed film.

S90-33961
John Gosbee is seen evaluating the function of a large spray bottle after the contains has been shaken and foam has formed inside the bottle. The photograph was taken with out a flash in an attempt to highlight the spray and the highlights from the fixed lighting. This photograph demonstrates how easy it is to cause foaming in microgravity. It appears that the device continues to work as seen by the faint white spray line in the center of the photograph. However, once no further liquid remains near the pickup straw in the bottle the device began to fail to product a full spray pattern. The Windex bottle could easily be operated with one hand.

S90-33962
In this photograph John Gosbee is seen operating the'Cetacaine Spray device with the Jetco nozzle under reduced lighting. As seen by the white spray line this device appeared to function throughout the flight. This device required the operator to use both hands, however it is believed that the operation of this device would be much easier if operated with out the large, bulky, rubber gloves. Once the gloves became wet the ability to hold onto items became harder.

S90-33988
This is another attempt at obtaining a photograph of the spray form the Ventolin Inhaler. During this attempt only the very beginning portion of the spray pattern can be seen at the opening of the inhaler mouthpiece.

S90-33989
Chuck Lloyd more clearly demonstrates the spray pattern obtained during

micro-gravity with the Cetacaine bottle. The spray pattern can be seen to cover from the nozzle opening to other side of the glove box, where the liquid coated the surface with benzocaine. The bottle required two hands to operate however it was easy to actuate the device.

S90-33990
Chuck Lloyd and Walter Cunningham evaluate the function of the Cetacaine Spray bottle during zero-g flight. The spray pattern can be seen from the opening of the nozzle to the other side of the glovebox.

S90-33992
From left to right, Kim Murray (Stella-Com), John Gosbee (KRUG), and Chuck Lloyd (NASA) floating during the last 5 parabolas of the Aerosol flight experiment. The set-up used for this experiment was placed in the front of the aircraft near where Kim is seen floating. The glovebox was secured to a table mounted to the floor up against one side of the aircraft. The high-speed camera was mounted on a pole in the center of the plane facing the center of the glovebox. A black sheet was hung from the ceiling in front of the camera so only the lenses struck through the sheet facing the glovebox. Lighting was placed around the end of the glovebox closest the front of the plane. The investigators performed their functions from the side furthest from the front of the plane. The camera and lighting was controlled form a rack near the front of the plane.

S90-33993
John Gosbee and Chuck Lloyd seen floating in the last 5 parabolas of the Aerosols experiment. The blackout curtain and the camera control rack can be seen in the background off to John Gosbee's right. The Medical Restraint System can be seen in the foreground to John's immediate right.

S90-33996
Chuck Lloyd more clearly demonstrates the spray pattern obtained during micro-gravity with the Cetacaine bottle. The spray pattern can be seen to cover from the nozzle opening to other side of the glove box, where the liquid coated the surface with benzocaine. The bottle required two hands to operate however it was easy to actuate the device.

S90-33998
Chuck Lloyd seen evaluating the standard nasal spray bottle during zero-g flight. The spray pattern can be seen as a broken white set of lines and drops from the nozzle of the bottle. The spray can be seen to about mid way in the glove box. This type of spray device appeared to work erratically.

It appeared to function best when the bottle was full based on its ability to delivery a mist type of spray pattern. By the time the bottle was 1/4 to 1/2 full the device began to only form bubbles at the nozzle tip or delivery a more liquid stream of fluid.

HIGH SPEED FILM

S90-023, 16mm, 200 feet, "A" Print, Aerosol Test, 1G.

S90-018, 16mm, "A" Print, Aerosol Spray Testing in Zero-G,Part 1 of 2.

S90-018, 16mm, "A" Print, Aerosol Spray Testing in Zero-G,Part 2 of 2.

VIDEO COPIES OF FILM:

Aerosol Spray Tests/ S90-023 & 018
Master Ref #118234
SMPTE (Window) time code.

code: AEROSOL1 on (NASA 10 disc OLD) NASA 16 9-17-89
Updated 2-26-90
Updated (Chg to AEROSOL2) 3-4-90
Updated 3-30-90
Updated 6-11-90 on NASA 19 disc
Updated 8-14-90
Updated 8-18-90 and moved to c:\word4\pcs\AEROSOL2 & NASA 19
Updated 11-29-90
Updated and reformated 4-8-91